CLAIMS

We claim:

1. A targeting construct comprising:

   (a) a first polynucleotide sequence homologous to at least a first portion of a PERK gene;

   (b) a second polynucleotide sequence homologous to at least a second portion of the PERK gene; and

   (c) a selectable marker.

2. A method of producing a targeting construct, the method comprising:

   (a) providing a first polynucleotide sequence homologous to at least a first portion of a PERK gene;

   (b) providing a second polynucleotide sequence homologous to at least a second portion of the PERK gene;

   (c) providing a selectable marker; and

   (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.

3. A cell comprising a disruption in a PERK gene.

4. The cell of claim 3, wherein the cell is a murine cell.

5. The cell of claim 4, wherein the murine cell is an embryonic stem cell.

6. A non-human transgenic animal comprising a disruption in a PERK gene.

7. The non-human transgenic animal of claim 6, wherein the transgenic animal is a mouse.

8. A cell derived from the transgenic mouse of claim 7.

9. A method of producing a transgenic mouse comprising a disruption in a PERK gene, the method comprising:

   (a) introducing the targeting construct of claim 1 into a cell;

   (b) introducing the cell into a blastocyst;

   (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

   (d) breeding the chimeric mouse to produce the transgenic mouse.

10. A method of identifying an agent that modulates the expression or function of a PERK gene, the method comprising:

(a) providing a non-human transgenic animal comprising a disruption in a PERK gene;

(b) administering an agent to the non-human transgenic animal; and

(c) determining whether the expression or function of the disrupted PERK gene in the non-human transgenic animal is modulated.

11. A method of identifying an agent that modulates the expression or function of a PERK gene, the method comprising:

(a) providing a cell comprising a disruption in a PERK gene;

(b) contacting the cell with an agent; and

(c) determining whether the expression or function of the PERK gene is modulated.

12. The method of claim 11, wherein the cell is derived from the non-human transgenic animal of claim 6.

13. An agent identified by the method of claim 10 or claim 11.

14. A transgenic mouse comprising a disruption in a PERK gene, wherein there is no significant expression of the PERK gene in the transgenic mouse.

15. A transgenic mouse comprising a homozygous disruption in a PERK gene, wherein the transgenic mouse exhibits a perinatal lethality.

16. A transgenic mouse comprising a homozygous disruption in a PERK gene, wherein the transgenic mouse exhibits a congenital abnormality.

17. The transgenic mouse of claim 16, wherein the congenital abnormality comprises hydrocephaly.

18. The transgenic mouse of claim 16, wherein the transgenic mouse exhibits an abnormality in an organ selected from the group consisting of lung, heart, pancreatic gland, stomach and liver.

19. A transgenic mouse comprising a heterozygous disruption in a PERK gene, wherein the transgenic mouse exhibits an increased susceptibility to seizure.

20. The transgenic mouse of claim 19, wherein the mouse exhibits seizure-like responses at a lower dose of Metrazol, relative to a wild-type mouse.

21. A cell derived from the transgenic mouse of claim 14.

22. A method of identifying an agent that ameliorates a phenotype associated with a disruption in a PERK gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a disruption in a PERK gene; and

(b) determining whether the agent ameliorates at least one of the following phenotypes: a perinatal lethality, a congenital abnormality, or an increased susceptibility to seizure.

23. An agent identified by the method of claim 22

24. An agonist or antagonist of PERK.